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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/511,037

01/19/2005

Klaus Michael Debatin

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EXAMINER

SANG, HONG

ART UNIT

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/511,037	<b>Applicant(s)</b> DEBATIN ET AL.	
	<b>Examiner</b> HONG SANG	<b>Art Unit</b> 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 06 May 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 35-43 and 45-52 is/are pending in the application.
- 4a) Of the above claim(s) 35-43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 45-52 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)             |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application   |
| Paper No(s)/Mail Date _____  | 6) <input checked="" type="checkbox"/> Other: <u>Exhibits A-C</u> . |

### DETAILED ACTION

**RE: Debatin et al.**

1. Applicant's response filed on 5/6/2008 is acknowledged.
2. Claims 35-43 and 45-52 are pending. New claims 45-52 have been added. Claims 1-34 and 44 have been cancelled. Claims 35-43 have been withdrawn from consideration.
3. Claims 45-52 are under examination.

***Rejection Maintained***

4. The rejection of claims 23-34 and 44 under 35 U.S.C. 103(a) as being unpatentable over Alnemri (WO 02/16418A2, Pub. Date: 2/28/2002, IDS), in view of Wang (WO 02/16402, Pub. Date: 2/28/2002, IDS), and Ford et al. (Gene Therapy, 2001, 8: 1-4) is withdrawn in view of applicant's cancellation of the claims. However, the same rejection is applied to the new claims 45-52 given that the new claims are claiming the same subject matter as the cancelled claims 23-34 and 44.

The response states that Ford teaches away from the subject matter of the present invention because Ford discloses that the full-length TAT protein stimulates growth of Kaposi's sarcoma-derived cells and that TAT transgenic mice develop Kaposi sarcoma, thus negating any apoptotic inducing effects of the Smac protein/or additional apoptotic inducing compounds. Moreover, Ford comment that the toxic effects of the protein *in vivo* is not known. The response further states that the examiner has failed to show any motivation for one skilled in the art to have selected TAT or fragments of TAT,

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over the other disclosed transducing polypeptides of Ford such as Antennapedia or the herpes simplex virus VP22 protein.

Applicant's arguments have been carefully considered but are not persuasive. While Fold discloses that the full-length TAT protein stimulates growth of Kaposi's sarcoma-derived cells and that TAT transgenic mice develop Kaposi sarcoma, Ford expressly teaches that PTD may provide efficient means of intracellular delivery of not just proteins, but macromolecules such as DNA as well as cancer chemotherapeutic agents (e.g. doxorubicin) (page 3, column 1, emphasis added). Fold teaches that protein transduction may also prove useful for efficient antigen loading of dendritic cells for a range of vaccination purposes, including anti-tumor immune therapy (see page 3, column 1, emphasis added). Therefore, Fold explicitly teaches the use of PTD for cancer drug delivery. Furthermore, one skilled in the art would have been motivated to use TAT PTD to deliver the Smac protein in view of Fold because Fold disclose that many proteins including small peptides have been successfully transported into a wide variety of human and murine cell type using the TAT PTD methodology (see page 2, column 2, 3<sup>rd</sup> paragraph). Whether one skilled in the art would have also been motivated to use Antennapedia or herpes simplex virus VP22 protein as a carrier protein for Smac is irrelevant to this rejection. Because of these reasons, the rejection is deemed proper and is therefore maintained.

It is noted that the amino acid sequence of the Smac-N7 taught by Alnemri is 100% identical to the amino acids 56-62 of the instant SEQ ID NO:1 (see sequence alignment Exhibit A). The amino acid sequence of the Smac-N35 taught by Alnemri

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comprises the amino acids 56-59, 56-62 and 56-70 of the instant SEQ ID NO.1 (see sequence alignment Exhibit B). The amino acid sequence of the AV peptide taught by Wang is 100% identical to the residue 56-62 of the instant SEQ ID NO.1 (see sequence alignment Exhibit C). While Ford does not specifically mention SEQ ID NO.3 recited in the claims, because Ford teaches the PTD domain of the TAT protein, the amino acid sequences disclosed in SEQ ID NO.3 is considered inherent property of the TAT protein.

### ***Objections and Rejections Withdrawn***

5. All other previous objections and rejections are withdrawn in view of applicant's cancellation of the claims, and submission the sequence listing and the Declaration to support filing and submission of the sequence listing.

### ***New grounds of objection***

#### ***Claim Objections***

6. Claim 46 is objected to because of the following informalities: claim 27 recite "amino acid sequence 47 to 57 SEQ ID NO: 3" (see step (ii), line 2). The term "of" should be added before the term "SEQ ID NO: 3".

#### ***Notice To Comply With Sequence Rules***

7. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a) (1)

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and (a) (2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicants fail to provide a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

### ***Conclusion***

8. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to HONG SANG whose telephone number is (571)272-8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Hong Sang/  
Examiner, Art Unit 1643  
9/2/08

/Christopher H Yaen/  
Primary Examiner, Art Unit 1643